DO

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,522	09/28/2001	Thomas Krahn	Bayer 10,139.3-KGB	5606

27384 7590 02/28/2006

NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,522	KRAHN ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-42* is/are pending in the application.

4a) Of the above claim(s) *6-16 and 24-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *6-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry & Claim Status

The amendment filed on October 20, 2005 has been acknowledged and entered.

Claims 6-42 are pending.

Claims 17-23 are examined.

Claims 6-16, 24-42 are withdrawn from further consideration.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-21, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cubbage et al. (US 5,582,982).

Wan teaches a method of using fluorescein conjugated E.Coli particles and second dye such as Trypan blue to quench the extracellular fluorescence in the solution. That means Trypan blue absorbs and the extracellular fluorescence which cause the solution to emit non-specific background light in the solution while the fluorescent that absorbs into the cells are being measured. Quenching the extracellular fluorescence thus means reducing non-specific background light in solution. (see

abstract, page 3 "Phagocytosis assay" and "results"). Trypan blue is obviously impermeant to the membrane of the cell because it quenches extracellular fluorescence. If it is permeable to the membrane, then it would quench all the fluorescence that absorbs into the cells and there would be no fluorescence left to detect. Wan also teaches that the concentration of trypan blue require to completely quench extracellular fluorescence was determined by exposing 3 or 6 $x10^8$ particles/well to serial dilutions of the dye in a 96-well plate. Complete quenching of the fluorescence was obtained with 250 ug/ml of the dye. Thus, Wan meets the requirement that the non-specific background in solution is reduced by at least 30%, 50% and 70% (claims 18-20). Since Wan teaches a fluorescent dye attached to the cell as in the present invention, such fluorescent dye is inherently permeant to the membrane of the cell and detects a voltage across the membrane of the cell. Since trypan blue can quench or reduce non-specific background, it would inherently be able to perform functions such as to improve the signal to noise ratio by at least 300%.

However, Wan fails to teach these reagents packaged in a kit.

Cubbage teaches a kit comprising a fluorescent probe and a background-reducing compound that diffuses into and onto the biological entity. (see col. 2, line 45-col. 7, line 27).

It would have been obvious to one of ordinary skills in the art package the components taught by Wan into a kit as taught by Cubbage for cost effective or other economic advantages.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cubbage et al. (US 5,582,982) as applied to claim 17-21, 23 above, and further in view of Van Aken (US 5,489,537).

Wan and Cubbage have been discussed above.

However, Wan and Cubbage fails to teach Brilliant Black as a fluorescent dye.

Van Aken teaches a method and kit for determining the presence or absence of a substance by detection of a colloidal dye associated with agglutinated particles. The colloidal dye is a background-enhancing dye, which reduces non-specific background to enhance optical detection. The background-enhancing dye is a water-soluble dye such as Brilliant Black. (see col. 21, lines 58-67).

It would have been obvious to one of ordinary skills in the art to use Brilliant Black as a masking or quenching dye in the kit for use in the method of Wan and Cubbage because both references teach using quenching or background reducing dye, which reduces background light in assay. Since Brilliant Black is known for enhancing the background in an assay, which uses optical detection, it would motivate one of ordinary skills in the art to use Brilliant Black in assays such as one taught by Wan and Cubbage because both Wan and Cubbage teach using fluorescent label, which is known for producing non-specific background.

Response to Arguments

Applicant's arguments filed on October 20, 2005 have been fully considered but they are not persuasive.

Applicants argue that if the fluorescent dye is attached to the cell, it cannot be permeant to the membrane of the cell. Second, the fluorescent dye recited in instant claims is unbound fluorescent dye, which is not conjugated to a cell. Third, Wan's fluorescein conjugated E. coli particles cannot be regarded as "fluorescent dye" and thus does not the terms of the present of the present claims, and, in any case, such particles are clearly not permeant to the membrane of any biological cell. Indeed, Wan expressly teaches that the particles are taken up by phagocytosis and they do not permeate any biological membrane.

Wan teaches that the fluorescein conjugated E. coli particles are added to the cells adhered to the bottom of the wells. Extracellular fluorescent was then quenched by adding trypan blue (masking dye). The intensity of the fluorescence associated with intracellular fluorescent particles was measured directly in the wells. (see abstract). Thus, although the fluorescein is conjugated to E.coli and in turn react with the cells adhered at the bottom of the wells, there exist intracellular fluorescence which implies that the dye must have permeated the membrane of the cells at the bottom of the wells in order to fluoresce intracellularly. Secondly, the claims recite an open claim language, comprising, and therefore fail to exclude any other substances attached to the fluorescent dye such as fluorescein conjugated E.coli particles. Phagocytosis can be a nonimmunological phagocytosis which refers to the ingestion of inert particles such as latex particles or of other particles that have been coated with a protein. Therefore, the

particles can be ingested by the cell and thus fluorescent dye can still permeate the cell membrane in order to produce intracellular fluorescence.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0923. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
January 05, 2006
PTD

Mary E. Ceperley

MARY E. CEPERLEY
PRIMARY EXAMINER
Acting SPE AU 1641